International Journal of Pathology; 2006; 4(2): 129-131

Case Report

Oxalosis in the Bone and Bone Marrow

Khalid Hassan, Javaid Hussain Qaisrani, Humaira Qazi, Lubna Naseem, Hasan Abbas Zaheer and Tahira Zafar

Department of Pathology, Pakistan Institute of Medical Sciences, Islamabad.

Introduction

Hyperoxaluria is characterized by supersaturation of calcium oxalate in the urine, and is strongly associated with nephrolithiasis and nephrocalcinosis. Oxalate is the salt form of oxalic acid and is a natural end product of glyoxylate metabolism. Oxalate does not appear to be needed for any human body process and normally more than 90% is excreted by the kidneys, with a small amount of excretion into the lower gut. Hyperoxaluria can result form excessive dietary intake of oxalates, overproduction of oxalates from the intestinal tract associated with intestinal diseases (enteric hyperoxaluria) and abnormalities in oxalate metabolism (primary hyperoxaluria)[1].

Long-standing and unattended hyperoxaluria can progressively impair renal functions, and ultimately lead to renal failure. This devastating phenomenon is characterized by oxalosis, a condition in which calcium oxalate crystals are deposited in the extrarenal organs. The common sites of oxalate deposition are the bones, bone marrow, blood vessels, central nervous system, peripheral nerves, retina, skin, and thyroid, etc[2].

Renal stones are a fairly common clinical entity. Many patients having renal stones present with renal colic and/or haematuria; however, an incidental diagnosis of nephrolithiasis on routine radiological examination is not uncommon. Since majority of cases of nephrolithiasis are not associated with metabolic oxalate defects, a metabolic screening for oxalate metabolism is usually not warranted in patients with their first renal stone. However, patients with recurrent renal stones and those presenting with renal calcinosis should be looked at with a strong clinical suspicion of underlying metabolic abnormalities[1].

Renal failure, which ensues with the passage of time in almost all the patients of oxalosis, is generally associated with anaemia. Deposition of oxalates in the bone marrow further aggravates anaemia and other cytopenias, and may cause leucoerythroblastic blood picture[3].

Here we report the case of a young adult having systemic oxalosis probably associated with late onset primary hyperoxaluria (PH). The patient presented with bilateral nephrolithiasis, obstructed uropathy, end stage renal disease and bicytopenia (anemia and thrombocytopenia). The histological diagnosis of oxalosis was made on bone marrow trephine biopsy.

Case Report

A 19 years old male patient presented with the history of vomiting and pain in both the legs. On physical examination he was found to be pale looking and there was no visceromegaly. Mild tenderness could be elicited on both the renal angles. There was no history of bowel symptoms or gastro-intestinal operation. Drug history was unremarkable. There was no history of chronic ascorbic acid ingestion.

When investigated through X-Rays KUB and ultrasound, it was noticed that his both kidneys contained multiple stones. With consequent obstructive uropathy, he had developed chronic renal failure. His urea was 387 mg/dl (N 15-40 mg/dl) while serum creatinin was 23.5 mg/dl (N <1.2 mg/dl). His serum calcium level was 9.1 mg/dl (N 9-11 mg/dl); serum phosphorus was 4.0 mg/dl (N 2.5-4.5 mg/dl); serum albumin was 3.4 g/dl (N 3.5-5.0 g/dl) and serum alkaline phosphatase was 30 u/l(N <38 u/l). His peripheral blood picture performed on haematology analyzer (Sysmex KX-21) showed Hb level of 8.4 g/dl; white cell count 5.2 x 10^9/l; and platelet count 116 x 10^9/l. The patient was

dialyzed twice and packed cells were given in an attempt to correct the anaemia.

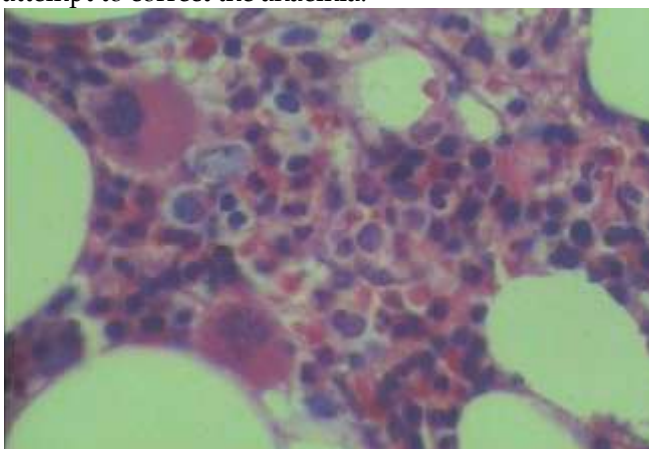

Figure 1: Trephine Biopsy Section showing Random Distribution of Erythroid, Myeloid and Megakaryocytic Series Cells (x400)

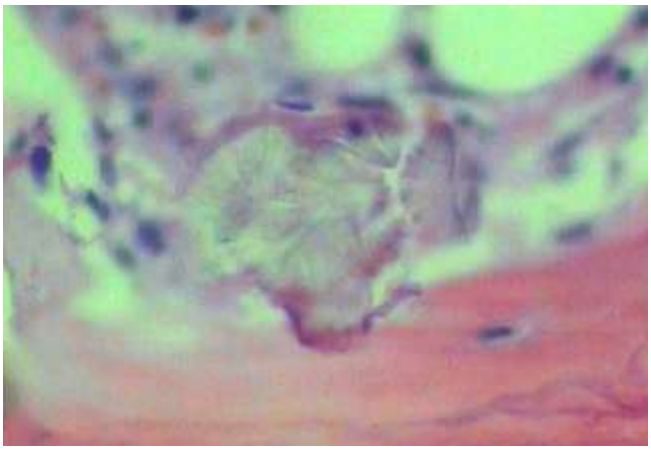

Figure 2: Trephine Section showing Deposition of Oxalate Crystal in the Bone Marrow (x400)

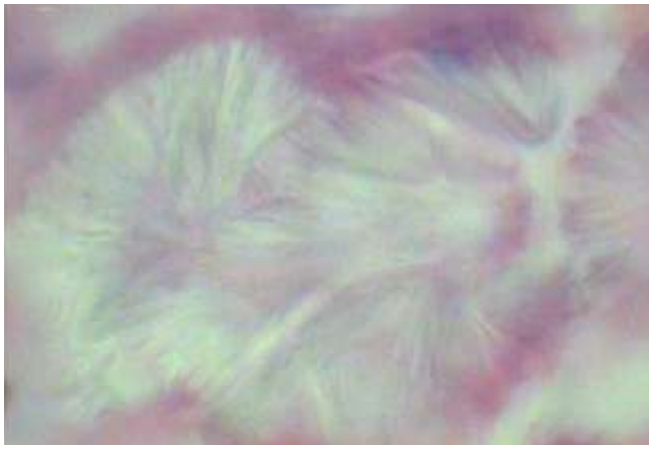

Figure 3: Trephine Section showing Deposition of Oxalate Crystal in the Bone (x1000)

Figure 4: Oxalate Crystals seen Through Polarized Light

On further probing into his family history it was found that one of his elder brothers also suffered from similar disease and later on had died with renal failure.

As the patient was being assessed for renal transplantation, and also had bicytopenia, he was referred to us, with a clinical suspicion of oxalosis, for bone marrow aspiration and trephine biopsy. Bone marrow aspiration and trephine biopsy revealed a moderately cellular marrow with some areas of hypocellularity.

In the moderately cellular areas, erythroid, myeloid and megakaryocytic series cells were randomly distributed (Figure 1). Erythropoiesis was normoblastic with moderate degree megaloblastic change. Bicytopenia was ascribed to this megaloblastic change and renal failure. At some places, in the bone trabeculae as well as in the bone marrow, oxalate crystals were observed in variable sized aggregates (Figure 2 & 3).

Discussion

In patients presenting with nephrolithiasis and those manifesting nephrocalcinosis, a strong clinical suspicion can lead to diagnosis of oxalosis at an early

stage[1]. However, if the disease is left undiagnosed, the results are devastating, and deposition of oxalates in renal as well as extra-renal tissues always occurs. It is associated with tissue damage and dysfunction.

Our patient was a young adult who presented rather late with widespread deposition of oxalates, as evidenced by nephrolithiasis, renal failure and morphologic evidence of oxalate deposition in bone and bone marrow. Since he presented late (at the age of 19 years), and also gave a history that one of his elder brothers had died of a similar illness, he was labelled as having late onset primary hyperoxaluria with oxalosis. Further, he was found to have bicytopenia (Hb 8.4 G/dl; and platelets 116 x 10^9/l). His trephine biopsy showed deposition of oxalates in the bone as well as bone marrow, however, sparing the bone marrow cells. Therefore, it was presumed that the bicytopenia was not causally related to oxalate deposition in the bone marrow. Anemia could be attributed to renal failure and megaloblastic change.

Hyperoxaluria can be secondary, primary or idiopathic. Secondary hyperoxaluria usually results from impaired renal excretion; excessive dietary oxalate intake with ascorbic acid[4] and ethylene glycol ingestion; or increased absorption in patients with chronic inflammatory bowel disease and intestinal by-pass[2]. Primary hyperoxaluria (PH) is also common, and is of two types: PH1 and PH 2. PH1 is more heterogeneous, more severe and more commonly associated with deposition of oxalate crystals in extra-renal tissues[2, 5].

Primary hyperoxaluria type1 (PH1) is an inherited defect (autosomal recessive) in glyoxylate metabolism caused by a deficiency in the liver specific enzyme known as alanine glyoxylate aminotransferase (AGT). The deficiency is due to mutation in AGT gene, located on chromosome 2q37.3 and results in the conversion of glyoxylate to oxalate. The crystallization of oxalate with calcium results in manifestations varying from a solitary kidney stone to end stage renal disease with systemic oxalosis[6]. PH1 is much more prevalent in Mediterranean countries accounting for 13.5% of end stage renal diseases compared with only 0.7% such disease in North America[7]. PH2 is caused by a defective glyoxylate reductase gene located on chromosome 9q11 resulting in increased oxidation of glyoxylate to oxalate[5]. Idiopathic hyperoxaluria has no known associated gene defect, and is usually linked with inherited oxalate over-production or abnormal membrane transfer of oxalate[8, 9].

Most patients with hyperoxaluria present with renal calculi at an early age. Our patient presented at 19 years age with bilateral nephrolithiasis, end-stage renal disease and bicytopenia (Hb 8.4 G/dl and platelet count 116 x10^9/l). Walter MJ[10] reported a similar case with pancytopenia secondary to oxalosis in a 20 years old female patient. The bone marrow biopsy in his patient revealed "extensive oxalate crystal deposition with almost complete obliteration of haemopoietic cells". Therefore, pancytopenia was correlated with deposition of oxalates in the bone marrow. On the contrary, in our patient, the oxalate deposition was relatively milder, thereby sparing haemopoietic series cells. The finding of bicytopenia was thus correlated with the megaloblastic change in addition to renal failure as a cause of anemia.

An early diagnosis of oxalosis is of immense value, because at a stage when renal failure has not set in, a proper management can arrest or at least delay the progress of disease. However, in patients who have already developed renal failure at the time of diagnosis of oxalosis, a combined liver and kidney transplantation offers the most effective treatment, because the new liver will have the capability of producing necessary enzymes and the new kidney will excrete oxalates normally[1,11]. Dialysis alone as a modality of treatment has been observed to be ineffective in retarding the disease progress, as the amount of oxalate production almost always surpasses the amount removable by dialysis, thereby leading to a positive balance in favour of oxalate deposition[12].

References

1. Wong PN, Tong GMW, Lo KY, Law ELK, Wong AKM. Primary hyperoxaluria: a rare but important cause of nephrolihtiasis. HKMJ 2002; 8: 202-206.
2. Alkhunaizi A and Chan L. Secondary oxalosis: a cause of delayed recovery of renal function in the setting of acute renal failure. J Am Soc Nephrol. 1996; 7: 2321-2326.
3. Bain BJ, Clark DM, Lamper IA and Wilkins BS. Bone marrow pathology. Blackwell science Ltd. Oxford 3rd edition. 2001; pp 422.
4. Mashour S, Turner JF Jr and Merrell R. Acute Renal Failure, Oxalosis, and Vitamin C Supplementation. Chest. 2000; 118: 561-563.
5. Kuo WL, Horton K and Fishman KE. CT evaluation of multisystem involvement by oxalosis. AJR. 2001; 177: 661-663.
6. Vanwoerdan CS, Groothof JW, Wanders RJ, Waterham HR, Wijburg FR. From gene to disease; Primary hyperoxaluria type! Caused by mutation in the AGXT gene. Ned Tijdschr Geneekd. 2006; 150(30): 1669-72.
7. Rinat C, Wanders RJA, Drukker A, Halle D, and Frishberg Y. Primary hyperoxaluria type 1: A model for multiple mutations in a monogenic disease within a distinct ethnic group. J Am Soc Nephrol. 1999; 10: 2352-2358.
8. Ruml LA, Pearle MS, Pak CYC. Urolithiasis. Uro Clin North Am. 1997; 24: 117-133.
9. Danpure CJ. Urolithiasis: genetic disorders and urolithiasis. Urol Clin North Am 2000; 27: 287-299.
10. Walter MJ and Dang CV. Pancytopenia secondary to oxalosis in a 23 years old woman (letter to editor). Blood. 1998; 91(11): 4394.

11. Cochat P, Gaulier JM, Koch PC et al. Combined liver kidney transplantation in primary hyperoxaluria type1. Eur J Pediatr 1999; 158[suppl]: 575-580.

12. Bunchman TE and Swartz RD. Oxalate removal in type 1 hyperoxaluria or acquired oxalosis using HD and equilibration PD. Perit Dial Int. 1994; 14: 81-84.